LDB3 gene

LIM domain binding 3

Normal Function

The *LDB3* gene provides instructions for making a protein called LIM domain binding 3 (LDB3). The LDB3 protein is found in heart (cardiac) muscle and muscles used for movement (skeletal muscle). Within muscle fibers, LDB3 proteins are found in structures called sarcomeres, which are necessary for muscles to tense (contract). This protein attaches (binds) to other proteins and is involved in maintaining the stability of rod-like structures within sarcomeres called Z-discs. Z-discs link neighboring sarcomeres together to form myofibrils, the basic unit of muscle fibers. The linking of sarcomeres and formation of myofibrils provide strength for muscle fibers during repeated cycles of muscle contraction and relaxation.

Several different versions (isoforms) of the LDB3 protein are produced from the *LDB3* gene.

Health Conditions Related to Genetic Changes

familial dilated cardiomyopathy

myofibrillar myopathy

At least three mutations in the *LDB3* gene have been found to cause myofibrillar myopathy. These mutations change single protein building blocks (amino acids) in the LDB3 protein. Mutated LDB3 proteins cluster together with other muscle proteins in the sarcomere to form clumps (aggregates). The aggregates prevent these proteins from functioning normally. A dysfunctional desmin protein cannot properly interact with Z-discs, leading to abnormalities of sarcomere structure and problems with the formation of myofibrils. *LDB3* gene mutations that cause myofibrillar myopathy impair the function of muscle fibers, causing weakness and the other features of this condition.

other disorders

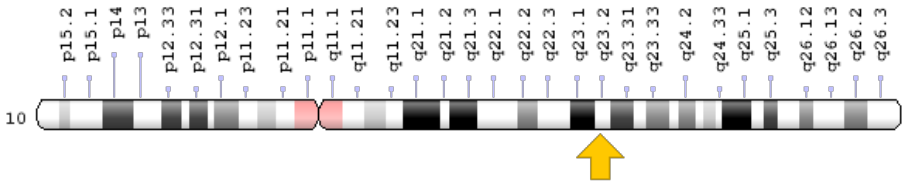
Mutations in the *LDB3* gene also cause a form of heart disease called dilated cardiomyopathy. This condition enlarges (dilates) and weakens the cardiac muscle, preventing it from pumping blood efficiently. Although cardiomyopathy is a sign of myofibrillar myopathy, some cases of dilated cardiomyopathy caused by *LDB3* gene mutations are not associated with weakness of the skeletal muscles. Researchers have identified at least two mutations in the *LDB3* gene that cause

dilated cardiomyopathy without the other features of myofibrillar myopathy. These mutations, written as Asp117Asn and Lys136Met, change single amino acids in the LDB3 protein. Researchers are not certain why some mutations in the *LDB3* gene cause dilated cardiomyopathy instead of myofibrillar myopathy.

Chromosomal Location

Cytogenetic Location: 10q23.2, which is the long (q) arm of chromosome 10 at position 23.2

Molecular Location: base pairs 86,664,785 to 86,736,072 on chromosome 10 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- LDB3_HUMAN
- LDB3Z1
- LDB3Z4
- LIM domain-binding protein 3
- ZASP

Additional Information & Resources

Educational Resources

- The Cell: A Molecular Approach (second edition, 2000): Muscle Contraction https://www.ncbi.nlm.nih.gov/books/NBK9961/#A1791
- Washington University, St. Louis: Neuromuscular Disease Center: Myofibrillar Myopathies http://neuromuscular.wustl.edu/musdist/lg.html#myofibzasp

GeneReviews

- Dilated Cardiomyopathy Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1309
- Myofibrillar Myopathy
  https://www.ncbi.nlm.nih.gov/books/NBK1499

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28LDB3%5BTIAB%5D%29+OR+%28LIM+domain+binding+3%5BTIAB%5D%29%29+OR+%28ZASP%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D

OMIM

- CARDIOMYOPATHY, DILATED, 1C, WITH OR WITHOUT LEFT VENTRICULAR NONCOMPACTION
  http://omim.org/entry/601493
- LIM DOMAIN-BINDING 3
  http://omim.org/entry/605906

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_LDB3.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=LDB3%5Bgene%5D
- HGNC Gene Family: LIM domain containing
  http://www.genenames.org/cgi-bin/genefamilies/set/1218
- HGNC Gene Family: PDZ domain containing
  http://www.genenames.org/cgi-bin/genefamilies/set/1220
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=15710
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/11155
- UniProt
  http://www.uniprot.org/uniprot/O75112

Sources for This Summary

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  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18764962
- OMIM: LIM DOMAIN-BINDING 3
  http://omim.org/entry/605906
- Schröder R, Schoser B. Myofibrillar myopathies: a clinical and myopathological guide. Brain Pathol. 2009 Jul;19(3):483-92. doi: 10.1111/j.1750-3639.2009.00289.x. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19563540
- Selcen D, Engel AG. Mutations in ZASP define a novel form of muscular dystrophy in humans. Ann Neurol. 2005 Feb;57(2):269-76.
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